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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/899,922	07/09/2001	Amanda Johanne Kiliaan	BO 44633	5229

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EXAMINER	
DAVIS, RUTH A	

ART UNIT	PAPER NUMBER
1651	

DATE MAILED: 11/01/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/899,922	KILIAAN ET AL.	
	Examiner	Art Unit	
	Ruth A. Davis	1651	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *25 August 2005*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *42-60* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *42-60* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

Applicant's Request for Continued Examination filed August 25.2005 and amendment filed June 27, 2005 have been received and entered into the case. Claims 42 – 60 are pending and have been considered on the merits. All arguments have been fully considered.

Claim Rejections - 35 USC § 112

1. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

2. Claims 42 – 58 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for a method for treating a person with unipolar depression, does not reasonably provide enablement for treating a person who is at risk of developing unipolar depression. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to practice the claimed method commensurate in scope with these claims.

The claims are drawn to methods for treating persons who have vascular disorders and also who are at risk of developing unipolar depression. Since applicant has not defined who is "at risk of developing unipolar depression", and the methods do not require that the person actually has unipolar depression, the claims are interpreted to encompass a method for preventing unipolar depression. Prevention provides for an expectation that a disease or disorder

does not occur in response to an initiating event. While there is no requirement that prevention must be absolute in all cases, there is a reasonable expectation that some element of prevention can be shown. The standard for showing prevention or preventative effects is very high. The standard of enablement is higher for inventions requiring prevention or preventative effects in disease conditions, since such effects may be unbelievable absent strong supporting evidence. Claims drawn to compositions with preventative effects generally require evidence because of the unpredictability in biological responses to therapeutic treatments.

Applicant has not provided convincing evidence that the claimed methods and compositions are preventative against unipolar depression. The specification is absent actual working examples of how the claimed composition exhibits preventative effects against the claimed conditions. The specification fails to teach one in the art how to administer the composition in terms of dose, duration and methodology such that one in the art could use the claimed extract to prevent the claimed disease. For example, there is no teaching of administering the claimed composition to subjects wherein unipolar depression is prevented. The specification further fails to particularly identify the treating population. Specifically, for who is at risk for developing the claimed disorder and does not identify who may in included or excluded in such a population. For example, the disclosure fails to set forth if the method is intended for the general population or for someone already suffering from depression or related disorders. It would place an undue burden of experimentation on the person of ordinary skill in the art to find suitable methodologies of administering the claimed composition, such that the claimed disorders would be prevented and/or treated. Thus, the specification fails to provide sufficient guidance to allow one in the art to use the claimed invention without undue

experimentation. Therefore, absent of such guidance and evidence, the specification fails to provide an enabling disclosure.

Response to Arguments

Applicants argue that the methods are drawn to treating someone who is at risk of developing unipolar disorder, not preventing it; that the specification identifies those considered to be at risk of developing unipolar depression (spec p3-5); and that one in the art would know who would be considered "at risk of developing' unipolar depression.

However, these arguments fail to persuade because as stated above, since applicant has not clearly defined who is "at risk of developing" unipolar depression, the methods are interpreted as preventing unipolar disorder. Moreover, the methods do not require the treating population to actually have unipolar disorder, but merely that they may or may not develope unipolar depression. Thus, the claims encompass a method for preventing unipolar disorder.

Regarding applicant's assertion that the treating population is identified and that one in the art would known who that population would be, the pages relied upon merely define depression and/or mood disorders, identifies causes of depression, and identifies groups of people who suffer from depression. The disclosure does not identify people who are at 'risk of developing unipolar depression", as claimed. Finally, even if one in the art might be able to determine who is "at risk", the specification still fails to teach one in the art how to treat a person who may or may not develop (or prevent) unipolar depression as stated here and in the above rejection.

Claim Rejections - 35 USC § 103

3. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

4. This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

5. Claims 42 – 48 and 51 – 60 are rejected under 35 U.S.C. 103(a) as being unpatentable over Horrobin, Fugh-Berman, Maggioni and Growdon.

Applicant claims a method for treating a person having a vascular disorder and has or is at risk of developing unipolar depression, the method comprising orally administering a composition comprising (a) long chain polyunsaturated fatty acids (PUFAs) comprising omega-3 and omega-6 fatty acids in an amount of at least 350 mg/day, (b) phosphatidylethanolamine and phosphatidylcholine, and one of phosphatidylserine or phosphatidylinositol; in a ratio of 0.5 – 20; and (c) at least one compound selected from folate, vitamin B12, B6, magnesium, zinc. The

composition further comprises hypericin or Withania somniera; 0.5 – 30g citrate; tryptophan or protein containing tryptophan; one of SAMe choline, betaine or copper; one of vitamin C, E, lipoic acid, selenium salt or carotenoids; ginkgo biloba extract; or vitamin D. The omega-3 fatty acids are selected from eicosapentaenoic acid (EPA) and docosahexaenoic acid (DHA) and the omega-6 fatty acids are selected from arachidonic acid (ARA) and dihomogamma linolenic acid (DGLA). The (c) portion contains both folate and vitamin B6. Specifically, the composition comprises at least 120 mg long chain PUFAs, 200mg phospholipids, 200 micrograms folate, 0.1 mg hypericin or 100 mg W. somnifera, and 500 mg citrate. The phospholipids are in the amount of 1 g/day. Applicant additionally claims a method for treating a person having a vascular disorder and has or is at risk of developing unipolar depression, the method comprising administering a composition comprising (a) 350 mg of long chain PUFAs wherein the omega-3 fatty acids are EPA and DHA, and the omega-6 fatty acids are AA and DHGLA at a ratio of 2.5 – 5.5:1; (b) at least 2 phospholipids selected from phosphatidylethanolamine and phosphatidylcholine, and one of phosphatidylserine or phosphatidylinositol; (c) a compounds selected from folate, vitamin B12, B6, magnesium, zinc. Specifically, at least 20 mg EPA, 50 mg DHA, 50 mg AA, 200 mg phospholipids, 200 mg folate, 0.2 mg hypericin or 500 mg W.somnifera, 100 mg Mg, 5 mg Zn, 2 mg vitamin B6, 2 micrograms B12 and 1 g citrate. Applicant finally claims the method wherein the composition comprises 350 mg long chain PUFAs; at least 2 phospholipids selected from phosphatidylethanolamine, phosphatidylcholine, phosphatidylserine or phosphatidylinositol; a compound selected from folate, vitamin B12, B6, magnesium, zinc; and 4 – 40 micrograms of vitamin D3.

Horrobin teaches compositions and methods for treating depression and anxiety, the compositions comprising DHA (p.3,4), ascorbic acid (vitamin C), vitamin E, beta carotene, selenium, zinc, and vitamin B6 (p.5,7, claims). The composition may further comprise EPA, DGLA, and AA, (p.6). Specifically, dosages of at least 350 mg DHA are combined with 250 – 2000 mg of the other named fatty acids (p.6). Examples further include vitamins of the B group, vitamin D, folic acid (folate), magnesium, and lipoic acid (examples).

Fugh-Berman teaches St. John's Wort, or hypericine (p.713), ginkgo biloba (p.715-16), vitamin B12, folate (p.721), SAMe, and tryptophan (p.722) improve depression and symptoms thereof.

Growdon teaches methods for treating depression and related disorders comprising administering lecithin (consists of phosphatidylcholine, phosphatidylethanolamine, and phosphatidylinositol, see attached "Soy Lecithin Fact Sheet") (abstract, col. 1-3).

Maggioni teaches phosphatidylserine for treating depression and symptoms thereof (abstract).

The above references do not teach a composition comprising all of the combined ingredients. However, at the time of the claimed invention, it would have been obvious to one of ordinary skill in the art to combine the instant ingredients for their known benefit, as disclosed by the cited references above, since each is well known in the art for their claimed purpose. Moreover, at the time of the claimed invention, one of ordinary skill in the art would have been motivated to combine each of the claimed ingredients together with a reasonable expectation for successfully treating depression. Since each of the claimed ingredients were known to have the same, claimed, therapeutic effects, one in the art would know that they are result effective

variables. Thus, while references do not teach the specific amounts or ratios as claimed, it would have been well within the purview of one of ordinary skill in the art to optimize amounts and/or ratios as a matter of routine experimentation. In addition, although the references do not specifically teach inclusion of citrate, citrate was a well known stabilizer and synergist with various vitamins (as admitted by applicant, specification p.5). It would have been obvious to one of ordinary skill in the art to include citrate as a matter of routine practice at the time the claimed invention was made. This rejection is based on the well established proposition of patent law that no invention resides in combining old ingredients of known properties where the results obtained thereby are no more than the additive effect of the ingredients, *In re Sussman,* 1943 C.D. 518. It is noted that where general conditions of a claim are disclosed in the prior art, it is not inventive to disclover the optimiun or workable ranges by routine experimentation. The normal desire of one in the art to improve upon what is already generally known provides the motivation to determine where in a disclosed set of ranges is the optimum combination (MPEP 2144)

Thus, the invention as a whole is *prima facie* obvious over the references, especially in the absence of evidence to the contrary.

6. Claim 49 is rejected under 35 U.S.C. 103(a) as being unpatentable over Horrobin, Growdon and Pollack.

Applicant claims a method for treating a person having a vascular disorder and has or is at risk of developing unipolar depression, the methodcomprising orally administering a composition comprising (a) long chain polyunsaturated fatty acids (PUFAs) comprising omega-3

and omega-6 fatty acids in an amount of at least 350 mg/day, (b) phosphatidylethanolamine and phosphatidylcholine, and one of phosphatidylserine or phosphatidylinositol; in a ratio of 0.5 – 20; and (c) at least one compound selected from folate, vitamin B12, B6, magnesium, zinc. The composition further comprises copper, with a ratio of zinc to copper of 5 – 12:1.

Horrobin teaches compositions and methods for treating depression and anxiety, the compositions comprising DHA (p.3,4), zinc, and vitamin B6 (p.5,7, claims). The composition may further comprise EPA, DGLA, and AA, (p.6). Specifically, dosages of at least 350 mg DHA are combined with 250 – 2000 mg of the other named fatty acids (p.6). Examples further include vitamins of the B group, folic acid (folate), magnesium, and lipoic acid (examples).

Growdon teaches methods for treating depression and related disorders comprising administering lecithin (consists of phosphatidylcholine, phosphatidylethanolamine, and phosphatidylinositol, see attached "Soy Lecithin Fact Sheet") (abstract, col. 1-3).

Pollack teaches methods for treating depression comprising administering compositions comprising vitamin B6 (pyridoxine), copper and magnesium (abstract, claims 8-14).

The above references do not teach a composition comprising all of the combined ingredients. However, at the time of the claimed invention, it would have been obvious to one of ordinary skill in the art to combine the instant ingredients for their known benefit, as disclosed by the cited references above, since each is well known in the art for their claimed purpose. Moreover, at the time of the claimed invention, one of ordinary skill in the art would have been motivated to combine each of the claimed ingredients together with a reasonable expectation for successfully treating depression. Since each of the claimed ingredients were known to have the same, claimed, therapeutic effects, one in the art would know that they are result effective

variables. Thus, while references do not teach the specific amounts or ratios as claimed, it would have been well within the purview of one of ordinary skill in the art to optimize amounts and/or ratios as a matter of routine experimentation. This rejection is based on the well established proposition of patent law that no invention resides in combining old ingredients of known properties where the results obtained thereby are no more than the additive effect of the ingredients, *In re Sussman,* 1943 C.D. 518. It is noted that where general conditions of a claim are disclosed in the prior art, it is not inventive to disclover the optimiun or workable ranges by routine experimentation. The normal desire of one in the art to improve upon what is already generally known provides the motivation to determine where in a disclosed set of ranges is the optimum combination (MPEP 2144)

Thus, the invention as a whole is *prima facie* obvious over the references, especially in the absence of evidence to the contrary.

7. Claim 50 is rejected under 35 U.S.C. 103(a) as being unpatentable over Horrobin, Growdon and Takeda.

Applicant claims a method for treating a person having a vascular disorder and has or is at risk of developing unipolar depression, the method comprising orally administering a composition comprising (a) long chain polyunsaturated fatty acids (PUFAs) comprising omega-3 and omega-6 fatty acids in an amount of at least 350 mg/day, (b) phosphatidylethanolamine and phosphatidylcholine, and one of phosphatidylserine or phosphatidylinositol; in a ratio of 0.5 – 20; and (c) at least one compound selected from folate, vitamin B12, B6, magnesium, zinc. The composition further comprises at least one of carnitine, B1, B5 or CoEnzyme Q10.

Horrobin teaches compositions and methods for treating depression and anxiety, the compositions comprising DHA (p.3,4), zinc, and vitamin B6 (p.5,7, claims). The composition may further comprise EPA, DGLA, and AA, (p.6). Specifically, dosages of at least 350 mg DHA are combined with 250 – 2000 mg of the other named fatty acids (p.6). Examples further include vitamins of the B group, folic acid (folate), magnesium, and lipoic acid (examples).

Growdon teaches methods for treating depression and related disorders comprising administering lecithin (consists of phosphatidylcholine, phosphatidylethanolamine, and phosphatidylinositol, see attached "Soy Lecithin Fact Sheet") (abstract, col. 1-3).

Takeda teaches compositions for treating depression comprising carnitine and vitamin B1 (abstract).

The above references do not teach a composition comprising all of the combined ingredients. However, at the time of the claimed invention, it would have been obvious to one of ordinary skill in the art to combine the instant ingredients for their known benefit, as disclosed by the cited references above, since each is well known in the art for their claimed purpose. Moreover, at the time of the claimed invention, one of ordinary skill in the art would have been motivated to combine each of the claimed ingredients together with a reasonable expectation for successfully treating depression. Since each of the claimed ingredients were known to have the same, claimed, therapeutic effects, one in the art would know that they are result effective variables. Thus, while references do not teach the specific amounts or ratios as claimed, it would have been well within the purview of one of ordinary skill in the art to optimize amounts and/or ratios as a matter of routine experimentation. This rejection is based on the well established proposition of patent law that no invention resides in combining old ingredients of known

properties where the results obtained thereby are no more than the additive effect of the ingredients, *In re Sussman,* 1943 C.D. 518. It is noted that where general conditions of a claim are disclosed in the prior art, it is not inventive to disclover the optimiun or workable ranges by routine experimentation. The normal desire of one in the art to improve upon what is already generally known provides the motivation to determine where in a disclosed set of ranges is the optimum combination (MPEP 2144)

Thus, the invention as a whole is *prima facie* obvious over the references, especially in the absence of evidence to the contrary.

Response to Arguments

Applicant first argues the references individually, in that they each do not disclose the claimed invention. Applicant additionally argues that the references do not teach the claimed amounts and ratios of phospholipids; that there is no motivation to combine and optimize the amounts of ingredients; that it is unexpected that the claimed diet is better than a diet without the supplement for treating depression; and that the examiner uses hindsight reasoning.

However, these arguments fail to persuade because one cannot show nonobviousness by attacking references individually where the rejections are based on combinations of references. See *In re Keller*, 642 F.2d 413, 208 USPQ 871 (CCPA 1981); *In re Merck & Co.*, 800 F.2d 1091, 231 USPQ 375 (Fed. Cir. 1986).

Regarding applicant's assertion that it would not be obvious to optimize the amounts and ratios of the instant ingredients, it is reiterated that it would have been well within the purview of

one of ordinary skill in the art to optimize the amounts and ratios of ingredients since they were known to have the claimed activity. It is specifically noted that Horrobin teaches a wide range of effective amounts of phospholipids (p.4,6,7) indicating that one in the art would recognize the ingredients as result effective variables. Thus one in the art would know to optimize the amount of such active ingredients. It is further noted that the ratios do not appear to impart unexpected advantages or results to the claimed composition.

Regarding applicant's claim that the instant composition is unexpectedly better, it is reiterated that the compositions described in the affidavit are not the same as the claimed composition, thus is not commensurate in scope with the claimed method. In order to provide convincing evidence of an unexpected advantage or benefit, the evidence must be commensurate in scope with the claimed composition and method.

Finally, in response to applicant's argument that the examiner's conclusion of obviousness is based upon improper hindsight reasoning, it must be recognized that any judgment on obviousness is in a sense necessarily a reconstruction based upon hindsight reasoning. But so long as it takes into account only knowledge which was within the level of ordinary skill at the time the claimed invention was made, and does not include knowledge gleaned only from the applicant's disclosure, such a reconstruction is proper. See *In re McLaughlin*, 443 F.2d 1392, 170 USPQ 209 (CCPA 1971).

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Ruth A. Davis whose telephone number is 571-272-0915. The examiner can normally be reached on M-H (7:00-4:30); altn. F (7:00-3:30).

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Michael Wityshyn can be reached on 571-272-0926. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Ruth A. Davis
October 21, 2005
AU 1651